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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,834	04/26/2006	Roberto A Macina	DEX-0532	8654

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EXAMINER
AEDER, SEAN E

ART UNIT	PAPER NUMBER
1642	

NOTIFICATION DATE	DELIVERY MODE
05/01/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

poreilly@licataandtyrrell.com

Office Action Summary	Application No.	Applicant(s)	
	10/523,834	MACINA ET AL.	
	Examiner	Art Unit	
	SEAN E. AEDER	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-22,25-30,33 and 34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-22,25-30,33 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/16/08; 2/19/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The Amendments and Remarks filed 1/24/08 in response to the Office Action of 8/24/07 are acknowledged and have been entered.

Claims 19-22, 25-30, 33, and 34 are pending.

Claims 19 and 37 have been amended by Applicant.

Claims 19-22, 25-30, 33, and 34 are currently under examination.

Objection Withdrawn

The objection to the specification is withdrawn.

Priority

It is again noted that the disclosure of the prior-filed Application No. 60/401,469 fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for all pending claims of this application. Note that Application No. 60/401,469 does not disclose antibodies, or antigen binding portions thereof, that are to bind and/or compete for binding to antigenic regions of instant SEQ ID NO:265 wherein said antigenic regions comprise the antigenic regions recited in independent claims 19 and 27. For instance, Application No. 60/401,469 does not disclose a limitation for antibodies that said antibodies bind and/or compete for binding to an antigenic region of instant SEQ ID NO:265 wherein said antigenic region comprises amino acid residues 71-83 of instant SEQ ID NO:265.

Response to Arguments

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 19, 20, 25, 27, 28, and 33 remain rejected under 35 U.S.C. 102(b) as being anticipated by Ashkar (WO 00/63247; 10/26/00) for the reasons stated in the Office Action of 8/24/07 and for the reasons set-forth below.

The Office Action of 8/24/07 contains the following text:

"The claims are drawn to compositions comprising antibodies, or antigen-binding portions thereof, that bind, and/or compete for binding to epitopes bound by antibodies that bind, antigenic regions of SEQ ID NO:265 wherein said antigenic regions are selected from the group consisting of: antigenic regions comprising amino acid residues 59-65 of SEQ ID NO:265; antigenic regions comprising amino acid residues 71-83 of SEQ ID NO:265; antigenic regions comprising amino acid residues 90-97 of SEQ ID NO:265; antigenic regions comprising amino acid residues 130-141 of SEQ ID NO:265; antigenic regions comprising amino acid residues 169-177 of SEQ ID NO:265; antigenic regions comprising amino acid residues 186-193 of SEQ ID NO:265; antigenic regions comprising amino acid residues 195-202 of SEQ ID NO:265; antigenic regions comprising amino acid residues 211-219 of SEQ ID NO:265; and antigenic regions comprising amino acid residues 226-240 of SEQ ID NO:265. It is noted that polypeptides comprising SEQ ID NO:265 are antigenic regions comprising the amino acid residues recited in the claims. Therefore, due to "comprising" language, antibodies that bind to any region of SEQ ID NO:265 would compete for binding to epitopes bound by antibodies that bind antigenic regions of SEQ ID NO:265 wherein said antigenic regions comprise the amino acid residues recited in the claims. Further, antibodies that bind to any region of SEQ ID NO:265 would bind antigenic regions of SEQ ID NO:265 wherein the antigenic region comprises the amino acid residues recited in the claims.

Ashkar teaches monoclonal and polyclonal antibodies against a fragment of osteopontin, set-forth as SEQ ID NO:3 (Leu-Val-Val-Asp-Pro-Lys) (see pages 7 and 17, in particular). It is noted that SEQ ID NO:3 is 100% identical to amino acids 214-219 of instant SEQ ID NO:265. Therefore, because the antibodies taught by Ashkar would bind SEQ ID NO:265, the antibodies taught by Ashkar would specifically bind antigenic regions *comprising* amino acid residues 59-65, 71-83, 90-97, 130-141, 169-177, 186-193, 195-202, 211-219, and 226-240 of SEQ ID NO:265. Further, the antibodies taught by Ashkar would specifically compete for binding to epitopes bound by antibodies which bind antigenic regions *comprising* amino acid residues 59-65, 71-83, 90-97, 130-141, 169-177, 186-193, 195-202, 211-219, and 226-240 of SEQ ID NO:265. Ashkar further teaches said antibodies conjugated to labels (see page 18 and Example 3, in particular). Ashkar further teaches compositions comprising said antibodies to be used to modulate tumor invasion and prevent or inhibit metastasis in human subjects with cancer (see page 22, in particular)."

In the Reply of 1/24/08, Applicant amended claim 19 to encompass antibodies, or antigen-binding portions thereof, that bind or compete for binding to epitopes bound by antibodies that specifically bind, antigenic regions of SEQ ID NO:265 wherein the antigenic regions to which the antibodies specifically bind are selected from the group consisting of: antigenic regions comprising amino acid residues 59-65 of SEQ ID NO:265; antigenic regions comprising amino acid residues 71-83 of SEQ ID NO:265; antigenic regions comprising amino acid residues 90-97 of SEQ ID NO:265; antigenic regions comprising amino acid residues 130-141 of SEQ ID NO:265; antigenic regions comprising amino acid residues 169-177 of SEQ ID NO:265; antigenic regions comprising amino acid residues 186-193 of SEQ ID NO:265; antigenic regions comprising amino acid residues 195-202 of SEQ ID NO:265; antigenic regions comprising amino acid residues 211-219 of SEQ ID NO:265; and antigenic regions comprising amino acid residues 226-240 of SEQ ID NO:265. Further, Applicant argues

that Ashkar does not teach antibodies with the ability to preferentially bind to "the defined" epitopes or antigenic regions.

The amendments to the claims and the arguments found in the Reply of 1/24/08 have been carefully considered, but are not deemed persuasive. In regards to the argument that Ashkar does not teach antibodies with the ability to preferentially bind to "the defined" epitopes or antigenic regions, polypeptides comprising SEQ ID NO:265 are antigenic regions comprising the amino acid residues recited in the claims. Therefore, antibodies that bind polypeptides comprising SEQ ID NO:265 would bind and compete for binding to epitopes bound by antibodies which specifically bind antigenic regions "comprising" the amino acid residues recited in the claims. The instant claims are not limited to antibodies and antigen-binding portions thereof that bind or compete for binding to epitopes bound by an antibody which specifically binds to an antigenic region "consisting of" any particular sequence.

Claims 19, 25-27, 33, and 34 remain rejected under 35 U.S.C. 102(e) as being anticipated by Muller et al (US US 2003/0118585 A1; filed 10/17/01) for the reasons stated in the Office Action of 8/24/07 and for the reasons set-forth below.

The Office Action of 8/24/07 contains the following text:

"Muller et al teaches polyclonal antibodies created by immunizing with the complete sequence of osteopontin (paragraphs 196-197, in particular). Muller et al further teaches the amino acid sequence of osteopontin as SEQ ID NO:23. It is noted that SEQ ID NO:23 is larger than instant SEQ ID NO:265; however, SEQ ID NO:23 comprises antigenic regions comprising amino acid residues 59-65 of instant SEQ ID NO:265 (see amino acids 130-136 of SEQ ID NO:23) antigenic regions comprising amino acid residues 71-83 of instant SEQ ID NO:265 (see amino acids 142-154 of SEQ ID NO:23); antigenic regions comprising amino acid residues 90-97 of instant SEQ ID

NO:265 (see amino acids 161-168 of SEQ ID NO:23); antigenic regions comprising amino acid residues 130-141 of instant SEQ ID NO:265 (see amino acids 201-212 of SEQ ID NO:23); antigenic regions comprising amino acid residues 186-193 of instant SEQ ID NO:265 (see amino acids 257-264 of SEQ ID NO:23); antigenic regions comprising amino acid residues 195-202 of instant SEQ ID NO:265 (see amino acids 266-273 of SEQ ID NO:23); antigenic regions comprising amino acid residues 211-219 of instant SEQ ID NO:265 (see amino acids 282-290 of SEQ ID NO:23); and antigenic regions comprising amino acid residues 226-240 of instant SEQ ID NO:265 (see amino acids 297-311 of SEQ ID NO:23). Therefore, due to homology between instant SEQ ID NO:265 and SEQ ID NO:23, the polyclonal antibodies taught by Muller et al would bind instant SEQ ID NO:265. Further, the polyclonal antibodies taught by Muller et al would bind epitopes bound by antibodies that bind antigenic regions of SEQ ID NO:265 comprising amino acid residues 59-65, 71-83, 90-97, 130-141, 169-177, 186-193, 195-202, 211-219, and 226-240 of instant SEQ ID NO:265. Muller et al further teaches said antibodies labeled and conjugated to a toxin for the treatment of tumors (see paragraphs 50-51 and 91-92, in particular)."

In the Reply of 1/24/08, Applicant argues that Muller et al only teaches methods for raising antibodies against the entire OPN protein (SEQ ID NO:24), amino acid domains 4-12 or 29-37 of SEQ ID NO:24, or non-define peptides of SEQ ID NO:24 (see paragraphs 196-197, in particular). Applicant further argues that Muller et al fails to teach any characteristics, such as the antigenic regions, of antibodies produced by Muller et al. Applicant concludes that Muller et al cannot anticipate claims drawn to antibodies that bind to specific regions of SEQ ID NO:265. Applicant further states that Muller et al does not teach antibodies with the ability to preferentially bind to "the defined" epitopes or antigenic regions.

The amendments to the claims and the arguments found in the Reply of 1/24/08 have been carefully considered, but are not deemed persuasive. In regards to the argument that Muller et al only teaches methods for raising antibodies against the entire OPN protein (SEQ ID NO:24), amino acid domains 4-12 or 29-37 of SEQ ID NO:24, or

non-define peptides of SEQ ID NO:24, polyclonal antibodies taught by Muller et al using a sequence encoding the entire OPN protein (SEQ ID NO:24) would bind regions throughout SEQ ID NO:23. It is again noted that SEQ ID NO:23 is larger than instant SEQ ID NO:265; however, SEQ ID NO:23 comprises antigenic regions comprising amino acid residues 59-65 of instant SEQ ID NO:265 (see amino acids 130-136 of SEQ ID NO:23) antigenic regions comprising amino acid residues 71-83 of instant SEQ ID NO:265 (see amino acids 142-154 of SEQ ID NO:23); antigenic regions comprising amino acid residues 90-97 of instant SEQ ID NO:265 (see amino acids 161-168 of SEQ ID NO:23); antigenic regions comprising amino acid residues 130-141 of instant SEQ ID NO:265 (see amino acids 201-212 of SEQ ID NO:23); antigenic regions comprising amino acid residues 186-193 of instant SEQ ID NO:265 (see amino acids 257-264 of SEQ ID NO:23); antigenic regions comprising amino acid residues 195-202 of instant SEQ ID NO:265 (see amino acids 266-273 of SEQ ID NO:23); antigenic regions comprising amino acid residues 211-219 of instant SEQ ID NO:265 (see amino acids 282-290 of SEQ ID NO:23); and antigenic regions comprising amino acid residues 226-240 of instant SEQ ID NO:265 (see amino acids 297-311 of SEQ ID NO:23). Therefore, polypeptides comprising SEQ ID NO:23 are antigenic regions comprising the amino acid residues recited in the claims. Further, due to homology between instant SEQ ID NO:265 and SEQ ID NO:23, the polyclonal antibodies taught by Muller et al would bind instant SEQ ID NO:265. Such polyclonal antibodies that bind polypeptides comprising SEQ ID NO:265 would bind and compete for binding to epitopes bound by antibodies which specifically bind antigenic regions "comprising" the amino acid residues recited in

the claims. The instant claims are not limited to antibodies and antigen-binding portions thereof that bind or compete for binding to epitopes bound by an antibody which specifically binds to an antigenic region "consisting of" any particular sequence.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 19-22, 25-30, and 33-34 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Ashkar (WO 00/63247; 10/26/00) as applied to claims 19, 20, 25, 27, 28, and 33 above, and further in view of Muller et al (US US 2003/0118585 A1; filed 10/17/01) *or* Queen et al (US Patent 5,693,762; 12/2/97) for the reasons stated in the Office Action of 8/24/07 and for the reasons set-forth below.

The Office Action of 8/24/07 contains the following text:

"The teachings of Ashkar are described above. Ashkar does not specifically teach humanized antibodies, chimeric antibodies, or compositions comprising antibodies and toxins. However, these deficiencies are rendered obvious or made up in the teachings of Muller et al or Queen et al.

Teachings of Muller et al are described above. Muller et al also teaches chimeric humanized monoclonal antibodies specific for osteopotin would be conjugated to toxins and used to treat cancer (paragraphs 50-51, 91-92, and 230, in particular).

Queen et al teaches methods for producing, and compositions of, chimeric and humanized immunoglobulins (see column 2-3 and 12-16 and column 1 lines 56-59, in particular). Queen et al further teaches antibodies conjugated to a variety of cytotoxic agents including radioisotopes, chemotherapeutic drugs commonly used in cancer treatments, and various other toxins for therapeutic purposes (see column 20, lines 1-35). Queen et al further teaches that, as compared to non-recombinant mouse

monoclonal antibodies and non-recombinant rabbit polyclonal antibodies, chimeric humanized antibodies are expected to (i) interact better with the human immune system (i.e. CDC and ADCC), (ii) reduce the HAMA response and (iii) the chimeric humanized antibodies will "presumably have a longer half-life more similar to naturally occurring human antibodies, allowing smaller and less fragment doses to be given" (see column 16, lines 6-26). Further, Queen et al teaches that chimeric antibodies have proven to be therapeutically successful in some instances (column 1 lines 56-59, in particular).

One of ordinary skill in the art at the time the invention was made would have been motivated to create compositions comprising toxic agents conjugated to chimeric humanized antibodies from the anti-osteopontin monoclonal antibodies taught by Ashkar because Ashkar teaches that said antibodies are to be used to treat cancer (see page 22, in particular) and: (1) Muller teaches compositions comprising toxic agents conjugated to chimeric humanized antibodies that specifically bind osteopontin would be used to treat cancer (paragraphs 50-51, 91-92, and 230, in particular) or (2) Queen et al teaches compositions comprising toxic agents conjugated to chimeric humanized antibodies would be used to deliver chemotherapeutic agents and various other toxic agents (see column 20, lines 1-35) and as compared to non-recombinant mouse monoclonal antibodies and non-recombinant rabbit polyclonal antibodies, chimeric humanized antibodies are expected to (i) interact better with the human immune system (i.e. CDC and ADCC), (ii) reduce the HAMA response and (iii) the chimeric humanized antibodies will "presumably have a longer half-life more similar to naturally occurring human antibodies, allowing smaller and less fragment doses to be given" (see column 16, lines 6-26). One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for creating compositions comprising toxic agents conjugated to chimeric humanized antibodies from the anti-osteopontin monoclonal antibodies taught by Ashkar because: (1) Muller et al teaches compositions comprising toxic agents conjugated to chimeric humanized anti-osteopontin antibodies (paragraphs 50-51, 91-92, and 230, in particular) or (2) Queen et al teaches how to make compositions comprising toxic agents conjugated to chimeric humanized antibodies (see lines 1-35 of column 20, in particular). Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results."

In the Reply of 1/24/08, Applicant repeats arguments that have been addressed above.

Summary

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. ' 1.136(a). A shortened statutory period for response to this Final Action is set to expire three months from the date of this action. In the event a first response is filed within two months of the mailing date of this Final Action and the advisory action is not mailed until after the end of the three-month shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. '1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than six months from the date of this Final Action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SEA

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Primary Examiner, Art Unit 1642